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ASSESSING THE VALIDITY OF A JAPANESE COHORT STUDY

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INTRODUCTION

Results of a Japanese cohort study published by Takeshi Hirayama (3-6) have been influential in the assessment of cancer risks of non-smoking women exposed to environmental tobacco smoke (ETS) through their husbands' smoking. We compared mortality projections, based on Japanese national death rates, with the reported cohort mortality. These comparisons revealed serious external and internal inconsistencies in the study results:

* Reported cohort death rates were lower than those for all Japan, apparently because mortality tracing was incomplete and death rates among those lost to follow-up were higher than among those traced.
* Cohort mortality deficits varied greatly among sub-cohorts defined by entry age and marital status.

These inconsistencies raise the possibility that selection biases are present in the data which might distort comparisons between exposed and non-exposed groups.

COHORT SELECTION AND FOLLOW-UP

* The cohort was recruited in the last quarter of 1965 from 49 geographic areas within 29 Health Center Districts in 6 Japanese prefectures.
* Of persons aged 40-79 in the survey areas, 95% were included in the cohort (prefecture range: 91% to 99%). "Only those persons found healthy" were recruited. The criteria for exclusion on health grounds were not reported.
* The age distribution of the cohort was similar to that of the 1965 Japanese population, except that the cohort under-represented the 70-79 age group.
* The cohort was followed for 16 years to the end of 1981. The number of subjects lost to follow-up was not reported.

LIFE TABLE PROJECTIONS

Hirayama reported that age-specific mortality rates in the cohort, for all causes of death and for specific causes, were similar to those in the Japanese population. In fact, crude death rates for the 16-year study period, calculated by dividing reported total deaths by person-years of observation, were substantially lower than what would be expected from national death rates (Table I).

We arrived at this conclusion by constructing mortality projections for the

cohort, based on standard demographic life table procedures. Japanese death rate statistics were obtained from U.N. Demographic Yearbooks (7) for all-cause mortality, and from the Gann Monograph (2) for cancer mortality. The life tables provide year-by-year projections of cumulative deaths and person-years by age at observation. Cause-specific mortality projections were obtained by applying cancer death rates to the person-year projections. For smoking-specific sub-cohorts, adjustments to the published death rates were made by using the reported cohort mortality ratios for smokers versus non-smokers.

MORTALITY IN PERSONS LOST TO FOLLOW-UP

Total reported deaths in the cohort were 16,000 fewer than total projected deaths. For males, reported deaths were 8,600 (22.5%) less than projected, and for females reported deaths were 7,400 (25.5%) less than projected.

From the reported numbers of deaths, we calculated the numbers of person years which would have been observed in the cohort if there had been 100% follow-up. At the end of the 16-year study period, the totals of these calculated person-years were 108,000 more than reported person-years for males, and 95,000 more than reported for females. Those differences show that follow-up of the cohort must have been less than 100%. This conclusion is derived entirely from the reported cohort deaths and person-years of observation, and is not in any way based on the life table projections. Assuming that on the average 8 years of observation were lost per untraced person, an estimated 25,000 subjects, or about 10% of the whole cohort, were lost to follow-up.

The life table projections suggest that some 16,000 cohort deaths were not traced. That number is 64% of the estimated 25,000 persons lost to follow-up, as compared with approximately 21% of reported deaths among the cohort members who,

TABLE I

CRUDE DEATH RATES PER 100,000 PERSON-YEARS

	Males			Females		
	Projected Rate	Reported Rate	% of Projected	Projected Rate	Reported Rate	% of Projected
All Cause	2,300	1,824	79*	1,409	1,069	76
All-site Cancer	575.3	500.4	87	329.9	263.4	80
Lung Cancer	86.6	81.3	94	24.9	21.1	85

* Reported crude death rate as a percentage of projected.

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according to our estimates, were not lost to follow-up. This mortality differential is a possible explanation for the differences between reported and projected death rates noted above. In fact it is the most likely reason, since the alternative explanations discussed below seem inadequate to account for differences of the magnitude observed.

OTHER EXPLANATIONS FOR MORTALITY DEFICITS

We considered whether the discrepancy between reported cohort death rates and national rates could be explained by sampling variation, by lower death rates in the geographic areas represented in the cohort, or by "healthy person" effects.

* The size of the cohort is too large for sampling variation to be a credible explanation. For example, a 95% confidence interval for the ratio of reported to projected all-site cancer mortality among women is 78% to 82%.

* Japanese vital statistics by prefecture show regional variations in cause- and age-specific death rates, but these prefectural statistics do not suggest that death rates in the cohort as a whole would have been substantially lower than national rates. Thus it seems unlikely that regional variations could explain rate differentials of the magnitude indicated by the life table projections.

* Since there were some exclusions from the cohort on health grounds, one would expect an initial healthy person effect. However, examination of the ratios of reported deaths to life table projections in intervals of the 16-year study period shows that there were still very substantial cohort deficits in the last years of the study, and it is unlikely that a healthy person effect would persist strongly for so long in a cohort with entry ages of 40 to 79 years.

THE NON-SMOKING MARRIED WOMEN COHORT

At the beginning of the study period, the cohort contained 91,540 non-smoking married women (NSMW). A total of 16,181 deaths were projected for the NSMW, and 9,106 were reported. For all-causes, all-site cancer, and lung cancer, the percentages of reported to projected mortality for the NSMW were 56%, 67%, and 72% respectively. The remarkable feature of these projections is that while the mortality deficits relative to projections are very large for the NSMW (44%, 33%, and 28% for all-causes, all-site cancer, and lung cancer respectively), they are quite small for all other women (3%, 6%, and 3% respectively).

To investigate whether this pattern could be due to marital mortality differentials, we constructed a life table based on 1975 Japanese marital status-specific death rates (2). The result of our analysis was that reported total deaths were 63% of projected for the NSMW sub-cohort, while the ratio for all other women was 96%. Thus it appears that marital mortality differentials can explain only a

small part of the differences between the NSMW and other women in the reported versus projected mortality deficits.

When we compared reported and projected lung cancer mortality for the NSMW by entry-age decade, another internal inconsistency became apparent. Reported lung cancer mortality was only 51% of projected for the 60-69 entry-age group, while for younger women (40-59 years at entry) reported mortality was 84% of projected.

CONCLUSIONS

In their monograph on the design and analysis of cohort studies, Breslow and Day (1) note that: "The validity of a cohort study depends fundamentally on complete ascertainment of the events of interest (e.g., cancer death) ... ." Our analyses strongly suggest that reported death rates in the Hirayama cohort were substantially lower than Japanese national rates because mortality among persons lost to follow-up was higher than among those successfully traced. If this explanation is correct, it is possible that biases exist in the data which might invalidate an observed relationship between exposure to ETS and mortality. Such biases could arise, for example, if there were more complete ascertainment of vital status among those exposed than among those not exposed. The striking internal inconsistencies described above, between sub-cohorts defined by marital status and entry age, reinforce these doubts about the validity of the study.

REFERENCES

1. Breslow NE, Day NE (1987) The Design and Analysis of Cohort Studies. IARC, Lyon
2. Gann Monograph on Cancer Research No. 26 (1984) Segi, M et al (eds). Japan Scientific Societies Press, Tokyo
3. Hirayama, T (1967) Internal Report. National Cancer Center Research Institute, Tokyo
4. Hirayama, T (1970) Interim Report of Medical Research on Human Cancer. National Cancer Center Research Institute, Tokyo
5. Hirayama, T (1981) British Med J 282:183-185
6. Hirayama, T (1984) Preventive Med 13:680-690
7. United Nations (1972, 1985) 1971 and 1983 Demographic Yearbooks. United Nations Press, New York